

Applicants: Francois Maltais et al.
Application No.: 10/798,766

REMARKS

The Claim Amendments

Claim 1 has been amended as follows: (i) Compounds of formula **II** are recited. Support for this amendment is found in original claim 2. (ii) R^z is defined as a hydrogen atom. Support for this amendment is found in paragraph [00101] on page 30 of the specification. (iii) each R^y is defined as an optionally substituted C_{1-4} aliphatic group. Support for this amendment is found in paragraph [00100] on page 29 of the specification. (iv) Z^1 is defined as N and Z^2 is defined as CH. Support for this amendment is found in paragraphs [0080] and [0083] on pages 26 and 27, respectively, of the specification. (v) $T_{(m)}R^1$ is defined as hydrogen. Support for this amendment is found in paragraph [0085] on page 27 of the specification. In addition, since R^1 is hydrogen, according to the proviso of original claim 1, U is defined as NH. (vi) Q is defined as $-C(O)N(R)-$ or $-C(O)O-$. Support for this amendment is found in original claim 5. (vii) R^3 is defined as being selected from hydrogen, $CH(R^7)R^5$, a 3-7 membered carbocyclyl, or an optionally substituted group selected from C_{1-4} aliphatic, a 3-6 membered heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or a 5-6 membered aryl or heteroaryl ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur. Support for this amendment is found in original claim 3. (viii) R^2 is defined as being selected from $(CH_2)_3R^5$, $(CH_2)_3CH(R^5)_2$, or $(CH_2)_3CH(R^7)CH(R^5)_2$. Support for this amendment is found in original claim 4. (ix) U is defined as NH. Support for this amendment is found in original claim 1.

Claims 2-6 have been canceled.

Claims 7-8 have been amended such that they are dependent upon claim 1.

Claim 11 has been amended such that the recited compounds are within the scope of amended claim 1.

Claims 14, 17, and 18 have been amended to add or remove claim text that was inadvertently deleted or added when the claims were previously amended.

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None of the amendments contain new matter. Their entry is requested.

The Response

The Restriction Requirement

The Examiner alleges that the elected species (compound I-51, see below) is unpatentable and that searching the additional “distinct” claimed species would constitute an unreasonable search burden. The Examiner has therefore limited the examination of the claimed subject matter to compound I-51, with the provision that the scope of the elected subject matter will be expanded should compound I-51 be found allowable. As pointed out previously, the search burden is not unreasonable because the claimed genus is well defined. Further, the entire subject matter of claim 1 has been searched by the European Patent Office and only five references of particular relevance were identified. The Examiner asserts that this fact is immaterial because international applications go through a different restriction practice and are not restricted based on the independent and distinct standard. The Examiner’s assertion is inapposite because the European Patent Office searched the full scope of the claimed genus, without any restriction of the claimed subject matter. Accordingly, applicants request that the Examiner search the full scope of the amended claims.

The claim objections

The Examiner has objected to claims 1-7, 9-12, and 14 for containing non-elected subject matter. Claims 2-6 have been canceled. Applicants request that the Examiner search the full scope of the currently pending claims because there is no search burden.

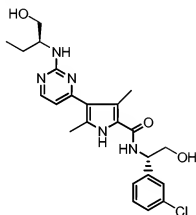
The rejection under 35 U.S.C. § 103(a)

The Examiner has rejected, in part, claims 1-7, 9-12, and 14 under 35 U.S.C. § 103(a) as allegedly being obvious over Cao et al., International Patent Publication No. WO

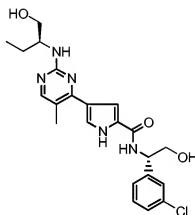
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2002/64586 (hereafter, "Cao"). Claims 2-6 have been canceled, thereby obviating the rejection of these claims.

In particular, the Examiner asserts that the elected species (compound I-51, see below) is *prima facie* obvious over Example 232 of Cao (see below). Consequently, the Examiner has limited the examined subject matter to that of compound I-51.



I-51



Example 232 of Cao

The Examiner reasons that hydrogen and methyl are deemed obvious variants in view of *In re Wood*, 199 USPQ 137. Furthermore, the Examiner asserts that it would have been obvious to one of ordinary skill in the art at the time the invention was made to follow the synthetic scheme of Cao and substitute methyl for hydrogen [or *vice versa*] where needed in the pyrimidine and pyrrole rings to make the claimed invention with a reasonable expectation of success. Applicants traverse.

The sole reason that the Examiner provides for Cao motivating one skilled in the art to make the necessary methyl for hydrogen and hydrogen for methyl substitutions is that both Cao and the present invention teach the use of compounds in the treatment of cancer. That alone is insufficient for establishing the *prima facie* obviousness of compound I-51 over Cao. In order to find a *prima facie* case of unpatentability in instances where close or established structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds, "a showing that the prior art would have suggested

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making the specific molecular modifications necessary to achieve the claimed invention [is] also required.” See *Takeda v. Alphapharm* (Fed. Cir. 2007), citing *In re Jones* (Fed. Cir. 1992); *In re Dillon* (Fed. Cir. 1990), *In re Grabiak* (Fed. Cir. 1985), and *In re Lulu* (Fed. Cir. 1984). “Thus, in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound” (emphasis added). See *Takeda v. Alphapharm*. Nothing in Cao provides such a reason.

There are 32 (2⁵) possible substitution patterns for pyrimidine-pyrrole rings analogous to compound I-51, where a hydrogen or methyl group can occupy one or more of the substitutable positions (including the pyrrole ring nitrogen atom). Compound I-51 is methylated at the pyrrole 3- and 5-positions but is not methylated at the pyrimidine 5-position, and thus exhibits three distinct changes from Example 232 of Cao. Nothing in Cao suggests making these particular changes. Cao exemplifies 238 compounds. None of these compounds has a pyrimidine-pyrrole substitution pattern corresponding to that of compound I-51. Further, not one of the compounds exemplified by Cao has even a single substituent on the pyrrole ring, much less two substituents, and only 11 compounds in Cao are unsubstituted at the pyrimidine 5-position. Therefore, the examples of Cao do not provide the required reasons to prepare compound I-51. Furthermore, the Examiner has not explained why Example 232 of Cao, which is methyl-substituted only at the pyrimidine 5-position, suggests making the specific molecular modifications required to produce compound I-51. Since compound I-51 is neither taught nor suggested by Cao, applicants respectfully request that the Examiner find claim 30 allowable and expand the examined subject matter to include that of amended claims 1, 7-12, and 14.

The rejections under obviousness-type double patenting

In a telephonic communication on November 13, 2007, the Examiner indicated that the terminal disclaimers over copending U.S. Patent Application Serial No. 10/770,814 and

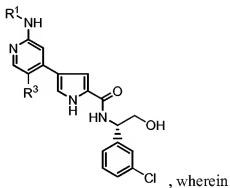
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U.S. Patent No. 6,743,791 have been approved by the U.S. Patent and Trademark Office. Accordingly, the obviousness-type double patenting rejections over these documents have been obviated.

The Examiner has provisionally rejected claims 1-7, 9-12, and 14 under the judicially created obviousness-type double patenting as being unpatentable over claims 1 and 22-23 of copending U.S. Patent Application Serial No. 11/128,870 (hereinafter "the '870 application") in view of Patani et al, *Chemical Reviews* 1996, 3147-3176 (hereafter, "Patani"), which teaches the bioisosteric replacement of nitrogen for carbon in a six-membered aryl ring. Claims 2-6 have been canceled, thereby obviating the rejection of these claims.

In particular, the Examiner asserts that it would have been obvious for one skilled in the art at the time the invention was made to follow the synthetic scheme of the '870 application, substitute methyl for hydrogen where needed in the pyrrole ring, and substitute nitrogen to replace the unsubstituted carbon in the 3-position of the pyridine ring to make the claimed invention with a reasonable expectation of success. Applicants traverse.

Pending claim 1 of the '870 application recites compounds having the formula:



R¹ is an optionally substituted C₁₋₆ aliphatic group and R³ is hydrogen, C₁₋₃ aliphatic, fluoro, or chloro. Each of the 26 exemplified compounds in the '870 application is substituted by a methyl or chloro group at R³ (the pyridine 5 position) and none of the exemplified compounds is substituted at the 3- or 5-positions of the pyrrole ring. Further, none of the compounds of the '870 application are pyrimidines. See compounds I-1 to I-18 on pages 10-

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11 and compounds II-1 to II-8 on page 25 of the '870 application. Thus, there are at least three distinct structural differences between the compounds in the '870 application and those claimed in the instant application. For the same reasons presented above in the argument against the 35 U.S.C. § 103(a) obviousness rejection, the '870 application does not provide any reasons for one skilled in the art to prepare compound I-51. Further, the Examiner has not explained why any of the pyridine/unsubstituted pyrrole-containing compounds of the '870 application or the teachings of Patani would suggest making the specific molecular modifications that are required to produce pyrimidine/dimethylpyrrole-containing compound I-51. Since compound I-51 is neither taught nor suggested by the '870 application in view of Patani, applicants respectfully request that the Examiner withdraw the obviousness-type double patenting rejection of claim 1, 7, 9-12, and 14 over claims 1 and 22-23 of copending U.S. Patent Application Serial No. 11/128,870 in view of Panani.

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Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying arguments, and find the elected species allowable. Applicants also request that the Examiner rejoin and examine the non-elected subject matter of claims 1, 7-12, and 14 of Restriction Group I, and allow these claims to pass to issue. Applicants further request that the Examiner rejoin and examine claims 15 and 17-18 of Restriction Group II and allow these claims to pass to issue as well. See MPEP § 821.04(b). Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the Examiner contact the undersigned at his convenience.

Respectfully submitted,

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